

In the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

Claims 1-37 (cancelled)

Claim 38 (original): A virion comprising a tissue-specific replication-conditional adenoviral vector comprising:

(a) a heterologous tissue-specific transcriptional regulatory sequence operably linked to the coding region of a gene that is essential for replication of said vector, wherein said coding region is an E1 a, E1b, E2, or E4 coding region; and

(b) at least one additional coding sequence encoding a heterologous gene product, wherein said additional coding sequence is operably linked to said heterologous tissue-specific transcriptional regulatory sequence.

Claim 39 (original): The virion of claim 38, wherein said tissue-specific transcriptional regulatory sequence is a promoter or an enhancer.

Claim 40 (original): The virion of claim 39, where said promoter is selected from the group consisting of an MUC1/DF3 promoter, an alpha-fetoprotein promoter, an erb-B2 promoter, a surfactant promoter, a thymidine kinase promoter, a p21 promoter, and a cyclin promoter.

Claim 41 (original): The virion of claim 39, wherein said enhancer is selected from the group consisting of DF3, a breast cancer-specific enhancer, viral enhancers, and steroid receptor enhancers.

Claim 42 (original): The virion of claim 38, wherein said additional coding sequence is selected from the group consisting of a thymidine kinase coding sequence, a cytosine deaminase coding sequence, and a purine nucleoside phosphorylase coding sequence.

Claim 43 (original): An isolated cell comprising the virion of claim 38.

Claim 44 (original): An isolated cell comprising the virion of claim 38, wherein said transcriptional regulatory sequence functions in said cell so that replication said cell

Claim 45 (original): The cell of claim 43, wherein said cell is a tumor cell or an abnormally proliferating cell.

Claim 46 (original): The cell of claim 45, wherein said additional coding sequence provides a gene product that provides anti-tumor activity in said cell.

Claim 47 (original): The cell of claim 45, wherein said tumor cell is selected from the group consisting of a hepatoma cell, and lung carcinoma cell.

Claim 48 (original): A method of producing the virion of claim 38, comprising culturing a cell infected with said virion and recovering said virion from said cell.

Claim 49 (original): The virion of claim 38, wherein said additional coding sequence expresses a gene product that can reduce or eliminate virion replication.

Claim 50 (original): The virion of claim 49, wherein said gene product is selected from the group consisting of cytosine deaminase, thymidine kinase, and purine nucleoside phosphorylase.

Claim 51 (original): A virion comprising a tissue-specific replication-conditional adenoviral vector comprising:

(a) a heterologous tissue-specific transcriptional regulatory sequence operably linked to the coding region of the adenovirus Ela gene that is essential for replication of said vector; and

(b) at least one additional coding sequence encoding a heterologous gene product, wherein said additional coding sequence is operably linked to a second transcriptional regulatory sequence that is activated by the E1 a gene product.

Claim 52 (original): The virion of claim 51, wherein said at least one additional coding sequence replaces a coding sequence of a gene in said vector, which gene is not essential for

vector replication, such that said at least one additional coding sequence is operably linked to and transcribed from said second transcriptional regulatory sequence.

Claim 53 (original): The virion of claim 51, wherein at least one of said transcriptional regulatory sequences is a promoter or an enhancer.

Claim 54 (original): The virion of claim 53, where said promoter is selected from the group consisting of an MUC1/DF3 promoter, an alpha-fetoprotein promoter, an erb-B2 promoter, a surfactant promoter, a thymidine kinase promoter, a p21 promoter, and a cyclin promoter.

Claim 55 (original): The virion of claim 53, wherein said enhancer is selected from the group consisting of DF3, a breast cancer-specific enhancer, a viral enhancer, and a steroid receptor enhancer.

Claim 56 (original): The virion of claim 51, wherein said additional coding sequence is selected from the group consisting of a thymidine kinase coding sequence, a cytosine deaminase coding sequence, and a purine nucleoside phosphorylase coding sequence.

Claim 57 (original): The virion of claim 51, wherein said at least one additional coding sequence encodes a gene product that can reduce or eliminate replication of said vector.

Claim 58 (original): The virion of claim 57, wherein said gene product is selected from the group consisting of cytosine deaminase, thymidine kinase, and purine nucleoside phosphorylase.

Claim 59 (original): An isolated cell comprising the virion of claim 51.

Claim 60 (original): An isolated cell comprising the virion of claim 51, wherein said transcriptional regulatory sequence operably linked to the coding region of the adenovirus Ela gene functions in said cell so that replication of said virion and expression of said additional coding sequence occurs in said cell.

Claim 61 (original): The cell of claim 59, wherein said cell is a tumor cell or an abnormally proliferating cell.

Claim 62 (original): The cell of claim 61, wherein said at least one additional coding sequence encodes a gene product that provides anti-tumor activity in said cell.

Claim 63 (original): The cell of claim 61, wherein said tumor cell is selected from the group consisting of a hepatoma cell and lung carcinoma cell.

Claim 64 (original): A method of producing the virion of claim 51, comprising culturing a cell infected with said vector and recovering said vector from said cell.

Claim 65 (original): The virion of claim 38, wherein said transcriptional regulatory sequence is a tumor-specific regulatory sequence.

Claim 66 (original): The virion of claim 65, wherein said tumor-specific regulatory sequence is a tumor-specific promoter.

Claim 67 (original): The virion of claim 38, wherein said transcriptional regulatory sequence is an alpha-fetoprotein promoter.

Claim 68 (original): The virion of claim 38, wherein said coding region is the E1a coding region.

Claim 69 (original): The virion of claim 38, wherein said coding region is the E1b coding region.

Claim 70 (original): The virion of claim 38, wherein said coding region is an E2 coding region.

Claim 71 (original): The virion of claim 70, wherein said coding region is the E2a coding region.

Claim 72 (original): The virion of claim 38, wherein said coding region is the E4 coding region.

Claim 73 (original): The virion of claim 38, wherein said additional coding sequence is a thymidine kinase coding sequence.

Claim 74 (original): The cell of claim 43, wherein said transcriptional regulatory sequence is a tumor-specific regulatory sequence.

Claim 75 (original): The cell of claim 74, wherein said tumor-specific regulatory sequence is a tumor-specific promoter.

Claim 76 (original): The cell of claim 43, wherein said transcriptional regulatory sequence is an alpha-fetoprotein promoter.

Claim 77 (original): The cell of claim 43, wherein said coding region is the Ela coding region.

Claim 78 (original): The cell of claim 43, wherein said coding region is the Elb coding region.

Claim 79 (original): The cell of claim 43, wherein said coding region is an E2 coding region.

Claim 80 (original): The cell of claim 79, wherein said coding region is the E2a coding region.

Claim 81 (original): The cell of claim 43, wherein said coding region is the E4 coding region.

Claim 82 (original): The cell of claim 43, wherein said additional coding sequence is a thymidine kinase coding sequence.

Claim 83 (original): The virion of claim 51, wherein said transcriptional regulatory sequence operably linked to the coding region of the adenovirus Ela gene is a tumor-specific regulatory sequence.

Claim 84 (original): The virion of claim 83, wherein said tumor-specific regulatory sequence operably linked to the coding region of the adenovirus Ela gene is a tumor-specific promoter.

Claim 85 (original): The virion of claim 51, wherein said transcriptional regulatory sequence operably linked to the coding region of the adenovirus Ela gene is an alpha-fetoprotein promoter.

Claim 86 (original): The virion of claim 51, wherein said at least one additional coding sequence replaces a coding sequence of the adenovirus E3 gene in said vector, such that said at least one additional coding sequence is operably linked to and transcribed from said second transcriptional regulatory sequence.

Claim 87 (original): The virion of claim 86, wherein said second transcriptional regulatory sequence is an adenovirus E3 promoter.

Claim 88 (original): The virion of claim 51, wherein said additional coding sequence is a thymidine kinase coding sequence.

Claim 89 (original): The virion of claim 87, wherein said additional coding sequence is a thymidine kinase coding sequence.

Claim 90 (original): The cell of claim 59, wherein said transcriptional regulatory sequence operably linked to the coding region of the adenovirus Ela gene is a tumor-specific regulatory sequence.

Claim 91 (original): The cell of claim 90, wherein said tumor-specific regulatory sequence operably linked to the coding region of the adenovirus Ela gene is a tumor-specific promoter.

Claim 92 (original): The cell of claim 59, wherein said transcriptional regulatory sequence operably linked to the coding region of the adenovirus Ela gene is an alpha-fetoprotein promoter.

Claim 93 (original): The cell of claim 59, wherein said at least one additional coding sequence replaces a coding sequence of the adenovirus E3 gene in said vector, such that said at least one additional coding sequence is operably linked to and transcribed from said second transcriptional regulatory sequence.

Claim 94 (original): The cell of claim 93, wherein said second transcriptional regulatory sequence is an adenovirus E3 promoter.

Claim 95 (original): The cell of claim 59, wherein said additional coding sequence is a thymidine kinase coding sequence.

Claim 96 (original): The cell of claim 94, wherein said additional coding sequence is a thymidine kinase coding sequence.